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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,576	07/24/1998	DANIEL V. SIEV	CVS-1	4548

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EXAMINER

EPPERSON, JON D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 08/21/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/122,576

Applicant(s)

SIEV ET AL.

Examiner

Jon D Epperson

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File Copy
-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 27 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,7-19,30 and 31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,8,9,13-19 and 30 is/are rejected.
- 7) ☒ Claim(s) 7,10-12 and 31 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 27, 2003 has been entered. Claims 1, 6-19 and 30-31 were pending (see Paper No. 22). Applicants cancelled claim 6 and amended claims 1, 7-8, 13, 15-16, 19, 30 and 31. Therefore, claims 1, 7-19 and 30-31 are pending and active in the instant application. An action on the merit follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. All previous objections and rejections are withdrawn in view of Applicants' arguments and/or amendments. The notice of allowability with regard to claims 6 and 12 and/or their incorporation into claim 1 is hereby withdrawn in view of the new art found on an update search (see rejection below).

New Rejections

Objections to the Claims

3. Claim(s) 7, 10-12 and 31 are objected to because of the following informalities:

A. Claims 10-12 and 31 are objected to as being dependent upon a rejected base claims, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8, 9, 13-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claim 8**, the phrase “wherein Y of reactant (b) in step (iv) is absent or is” is vague and indefinite. For example, it is not clear what Applicant means because reactant (b) in step (iv) has no “Y” i.e., reactant (b) has formula $R1-(C=X)-R2$. Applicants are requested to clarify. Therefore, claims 8 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. For **claim 9**, the phrase “the derivatized resin (TB)” is vague and indefinite. For example, it is not clear what Applicant means because reactant “(TB)” is not referred to in the claim. Does Applicant mean “(IB)”? Applicants are requested to clarify. Therefore, claims 8 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

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C. For **claim 13**, the phrase “represented by the formula (ID)” is vague and indefinite. For example, it is not clear what Applicant means because “formula (ID)” is not referred to in claim 13 or claim 1 from which it depends. Applicants are requested to clarify. Therefore, claims 13 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Shannessy et al (U.S. Patent No. 4,874,813) (Date of Patent is **October 17, 1989**) and Carey et

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al (Carey, F. A.; Sundberg, R. J. Advanced Organic Chemistry 3rd Ed. New York: Plenum Press. 1990, pages 146-147) and Chu et al (U.S. Patent No. 3,873,514) (Date of Patent is **March 25, 1975**).

For *claims 1 and 30*, O'Shannessy et al (see entire document) teaches a method for making Applicants' claim resin of Formula I wherein R₄ is NH₂, X is oxygen, Y is absent and Z is oxygen (see O'Shannessy et al, columns 5 & 6, especially column 6, lines 50-55).

The prior art teachings of O'Shannessy et al differ from the claimed invention as follows:

For *claims 1 and 30*, O'Shannessy et al is deficient in that it does explicitly teach the use of a R₁-C(=X)-R₂. For example, O'Shannessy does not teach the use of a coupling agent like carbonyldiimidazole wherein R₁ and R₂ are imidazole rings and X is oxygen. O'Shannessy et al only teaches the use of carbodiimides like 1-ethyl-3-(3'-dimethylaminopropyl)-carbodiimide (see O'Shannessy et al, column 5, line 16) that do not have the requisite R₁-C(=X)-R₂ formula.

However, the combined teachings of Chu et al and Carey et al teach the following limitations that are deficient in O'Shannessy et al:

For *claims 1 and 30*, the combined teachings of Chu et al and Carey et al (see entire document) teach the use of carbonyldiimidazoles with the requisite R₁-C(=X)-R₂ formula to produce the same N-hydroxy succinimide ester intermediates disclosed by O'Shannessy et al. For example, Chu et al (to which O'Shannessy et al incorporates by

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reference, see O'Shannessy et al, column 5, line 12) discloses that any carbodiimide can be used to produce the succinimide esters that are formed in O'Shannessy et al.

Furthermore, Carey et al teaches that carbonyldiimidazoles are particularly well suited for preparing these N-hydroxy succinimide ester intermediates using carboxylic acid starting materials because according to Carry carbodiimidazoles have a weak amide bond and are activated by protonation of the imidazole ring (see Carey et al, pages 146-147).

Therefore the combined teachings of O'Shannessy et al, Chu et al and Carey et al teach Applicants' claimed method. In this scenario, R-Y-Z-SS contains and agarose/linker solid support, a terminal oxygen for Z, no Y and a hydrogen for R (i.e., R-Y represent the terminal hydroxy group of the carboxylic acid). The R group is a leaving group and is thus deprotonated (i.e., the hydrogen is removed) to allow the oxygen to react with an R1-(C=X)-R2 compound (i.e., the carbonylcarbodiimide wherein both R1 and R2 are imidazole rings and X is an oxygen) as required by Applicants' claims. When the carboxylic acid reacts with the carbonylcarbodiimide an isolatable imidazolidine intermediate is formed (i.e., R1-(C=X)-Y-Z, wherein R1 is an imidazole ring, X is oxygen, Y is absent and Z is oxygen). This imidazolidine intermediate i.e., R1-(C=X)-Y-Z-SS (which represents Applicants compound (C)) then reacts with hydrazine hydrate (which represent Applicants compound (D) wherein R4 is NH₂) to yield a compound with general formula I (please note that the formation of an N-hydroxy-succinimide ester does not negate this process from falling within Applicants' claimed scope because Applicants use "comprising" terminology and thus more method steps may be added).

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It would have been obvious to one skilled in the art at the time the invention was made to use carbonyldiimidazole as taught by the combined teachings of Chu et al and Carey et al with the method steps taught by O'Shannessy et al because O'Shannessy et al explicitly incorporates the Chu et al reference in its entirety (see O'Shannessy et al, column 5, line 12). Furthermore, Chu et al teaches that any carbodiimide can be used in the method for forming N-hydroxy succinimide esters (see Chu et al, column 5, last paragraph), which would include the carbonylcarbodiimides taught by Carey et al. Furthermore, one of ordinary skill in the art would have been motivated to use the carbonylcarbodiimide taught by Carey et al because they are mild selective agents that react quickly with carboxylic acids because of their weak amide bonds and good protonated imidazole leaving group (see Carey et al, pages 146-147).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (703) 308-2423. The examiner can normally be reached Monday-Friday from 8:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-2439.

Jon D. Epperson, Ph.D.
August 9, 2003

BENNETT CELSA
PRIMARY EXAMINER

